papillary thyroid carcinomas (TCPTC); and 21 follicular thyroid carcinomas (FTC). All patients were managed according to a standard protocol based on current guidelines and followed-up for 116.9±70.8 months. VEGFA protein expression did not differentiate benign from malignant thyroid nodules. However, VEGFA was more frequently expressed in the less differentiated thyroid tissues. In fact, 95.8% of the FTC had positive expression. On the contrary, the intensity of this protein expression was progressively lower according to the process of cellular dedifferentiation (Goiter: 21.4%; FA: 16.3%; PTC: 8.7% and FTC: 0.0%; $x^2 = 0.031$). There was no difference in VEGFR2 expression between malignant and benign nodules ($x^2 = 0.108$), but this protein showed more intense expression in tissues that also presented Hürthle cells ($x^2 < 0.0001$). We were not able to find any correlation, neither of VEGFA nor with VEGFR2 expression, and any other feature of aggressiveness, including invasion, metastasis, lymph node metastasis, and distant metastasis. We conclude that VEGFA and VEGFR2 expression may help identify less differentiated tumors and the analysis of a larger cohort may prove the clinical utility of these markers.

Thyroid
BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Characteristics of Hypothyroid Patients Achieving Long Term Euthyroidism on Levothyroxine Treatment

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SAT-425
Characteristics of Hypothyroid Patients Achieving Long Term Euthyroidism on Levothyroxine Treatment
Background
Studies have shown that hypothyroid patients treated with Levothyroxine replacement therapy often experience fluctuations in TSH levels, while others remain well controlled over time.
Aim
To assess the association between pre-treatment TSH and other biochemical and clinical characteristics and long-term maintenance of normal TSH under Levothyroxine treatment.
Methods
This is a retrospective nested case-control study. Study population included patients above age 18 insured by Clalit Health Service (CHS) in the South of Israel between the years 2002-2017, diagnosed with hypothyroidism (ICD 9 code 244.9) and who had at least one TSH measurement before initiating levothyroxine therapy, purchased this medication for at least 5 consecutive years with one annual TSH measurement while on treatment. Patients with surgical, post iodine ablation or congenital hypothyroidism were excluded. Patients with a TSH level within the normal range for 5 consecutive years were defined as cases while the others served as controls. Demographic, laboratory, pregnancy status and pharmacy purchase were extracted from the computerized medical records of CHS and compared between the groups.
Results
Out of 5472 patients included in the study, 644 had a normal TSH for 5 consecutive years (11.8%, cases). Mean age at first levothyroxine purchase was 55.8±13.7 in cases and 54.10±16.2 in controls (p=0.003) and females comprised 84.8% and 81.4% respectively (p=0.035). Mean pretreatment TSH was 5.15±9.6 in cases and 10.02±29 in controls (p<0.001). Thyroid autoantibodies (anti TPO or anti thyroglobulin) were available in 40.8% and 44.8% of cases and controls respectively (P=0.63) and were positive in 36.5% and 56.7% (p<0.01). Subclinical hypothyroidism was diagnosed in 44.4% of cases and 54.6% of controls with prior to treatment. The odds ratio (OR) for having normal TSH for at least 5 consecutive years, using multivariable logistic regression was 0.99 for pretreatment mean TSH (p=0.89), 0.48 for positive thyroid antibodies (p<0.001), 0.72 for pretreatment diagnosis of subclinical hypothyroidism (p=0.032), 0.69 for use of iron supplements and 1.01 for age at first levothyroxine purchase (per year, p=0.02).
Conclusions
In our study population of adults with hypothyroidism treated with levothyroxine, only 11.8% were controlled for at least 5 consecutive years. Positive thyroid autoantibodies, pretreatment subclinical hypothyroidism and use of iron supplements lowered probability of long term TSH normalization, while age was associated with the increased rate. Further research should test whether TSH control for 5 consecutive years signals simply "good contol", or perhaps the possibility of transient forms of hypothyroidism for which treatment discontinuation is recommended.

Diabetes Mellitus and Glucose Metabolism
METABOLIC INTERACTIONS IN DIABETES

Dynamic and Regional Variation of Pancreatic Innervation in Diabetes

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SUN-654
Background: The pancreas is a highly heterogeneous organ, with regional anatomical, developmental and functional differences. The endocrine pancreas is densely innervated, and neural signals play a significant role in glucose regulation by modulating pancreatic hormone release. However, relatively little is known about the anatomical relationships between islets and nerves across the whole pancreas. Since thin filamentous structures, such as nerves, are difficult to quantify and trace over

large volumes using thin section histology, there is a need for high resolution imaging and rendering of intact pancreatic tissue in 3D. **Aim:** To use optical clearing, whole organ imaging, and 3D rendering to quantify islets and innervation across the whole pancreas in healthy mice, in two mouse models of diabetes, and in pancreatic samples from nondiabetic and diabetic human donors. **Methods:** Whole-mount staining and clearing was performed using iDISCO+ to quantify innervation, defined by the neuronal marker NF200, and beta cells in pancreata from C57Bl/6 mice, non-obese diabetic (NOD) mice, streptozotocin (STZ)-treated mice, and in pancreatic samples from nondiabetic and diabetic human donors. Z-stacked optical sections were acquired with an Ultramicroscope II at 4x or 12x magnification. Imaris was used to create digital surfaces covering the NF200+ innervation and islets to automatically determine innervation density and islet/nerve interactions. **Results:** Beta cell volumes were 1-4% in the human pancreas, and 1-2% in the healthy mouse pancreas, with regional variations in islet volume and insulin intensity. There were also significant differences in islet biology between the diabetes models. Innervation of the endocrine pancreas was significantly enriched compared to the surrounding exocrine pancreas, with regional variation. Islets were closely associated with pancreatic innervation and decreased in size with increasing distance from nerves in both mouse and human pancreatic tissue. Innervated islets were relatively preserved in models of diabetes. Finally, islet innervation and expression of neural markers were higher in human samples from diabetic patients and in mouse models of diabetes, with temporal and regional differences. **Conclusions:** 3D imaging and unbiased analysis across the whole pancreas provides comprehensive measurement of pancreatic nerve volumes and distribution. It allows detailed analysis of the anatomical relationship between nerves and islets, and reveals a close association that is maintained across species. The relative enrichment of innervated islets in diabetes and dynamic changes in islet innervation during the development of diabetes suggest further work is needed to examine the role of pancreatic nerves in preserving and protecting beta cells.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

The Effects of a High Intensity Glycemic Program on Weight and BMI

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MON-632
Background:
Multiple studies have shown that intensive glycemic control leads to improved HbA1c and delays the onset of complications in diabetes.[1] However, improvement in glycemic control has also been associated with weight gain.[1] The High A1C (HAC) program uses a multidisciplinary team to provide intensive therapy to patients with HbA1C

≥ 10% over 3 months to improve glycemic control. The aim of this retrospective study is to examine if the HAC program is associated with a significant change in weight and BMI.
Methods:
Patients enrolled in the HAC program were scheduled for frequent visits over the course of 3 months with an Endocrinologist, nurse practitioner, or diabetes educator. Data from patients with type 2 diabetes enrolled from March 2018 to June 2019 who attended at least 2 appointments was collected. Pre-enrollment HbA1c, weight, BMI, and total daily dose (TDD) of insulin (units/kg/day) were compared to post-enrollment using t-test analysis. Use of weight-lowering anti-hyperglycemic agents such as Metformin, GLP-1 agonists (GLP1A) and SGLT-2 inhibitors (SGLT2i) was collected.
Results:
44 patients were enrolled with 39/44 (88.6%) attending at least 2 visits and 5/44 (11.3%) who were lost to follow-up. The median HbA1c improved from 11.5% (9.7-14%) to 8.4% (5.9-14%), p<0.001. There was no significant change in mean weight (195lbs (110-360) vs 192lbs (114-358), p=0.14) or BMI (31 (20-49) vs 31 (21-49) kg/m^2, p=0.86). Pre-enrollment, 33/39 (84.6%) patients were on Metformin, 10/39 (25.6%) were on a GLP1A, and 3/39 (7.7%) were on a SGLT2i. At the end of the program, there were 34/39 (87%) patients on Metformin, 26/39 (66.6%) on a GLP1A, and 17/39 (43.5%) on a SGLT2i. There was no difference in the mean TDD of insulin at the start of the program of 0.63 units/kg/day (0-3.52 units/kg/day) compared to 0.60 units/kg/day (0-4.07 units/kg/day) at the end of the program (p=0.97).
Conclusions:
Patients enrolled in a high intensity glycemic control program had significant improvements in HbA1c without change in weight or BMI. Additional adjunctive non-insulin therapies and lifestyle management may be contributing factors for weight neutrality in our population. The significant improvement in HbA1c was not linked with increases in TDD of insulin.
Citation:
1. "U.K. Prospective Diabetes Study Group: Intensive blood glucose control with sulfonylureas or insulin compared with convention treatment and risk of complications in patients with Type 2 Diabetes." *Lancet*, vol.353, 1998, pp.837-53.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Linking Gonadotropin-Regulated Testicular RNA Helicase (GRTH/DDX25) to Histone Ubiquitination Network and Acetylation During Spermiogenesis

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SAT-031
Gonadotropin Regulated Testicular Helicase (GRTH/DDX25), a testis specific RNA helicase essential for the completion of spermatogenesis. Our early studies